

*Padgett et al.*  
Serial No.: 10/066,390  
Page 2 of 11

**AMENDMENTS TO THE CLAIMS;**

This listing of claims will replace all prior versions and listing of the claims in the application:

**LISTING OF THE CLAIMS:**

Claims 1-65 (canceled).

Claim 66. (previously presented) An in vitro method of making linear sequence variants from at least one heteroduplex polynucleotide where said heteroduplex has at least two non-complementary nucleotide base pairs separated by complementary nucleotide base pairs, said method comprising:

- a. preparing at least one heteroduplex polynucleotide;
- b. combining said heteroduplex polynucleotide with an effective amount of CEL I, T4 DNA polymerase, and T4 DNA ligase; and
- c. allowing sufficient time for the percentage of complementarity to increase, wherein one or more sequence variants are made.

Claim 67. (currently amended) An in vitro method of making linear sequence variants from at least one heteroduplex polynucleotide wherein said heteroduplex has at least two non-complementary nucleotide base pairs separated by complementary nucleotide base pairs, said method comprising:

- a. preparing at least one heteroduplex polynucleotide;

*Padgett et al.*  
Serial No.: 10/066,390  
Page 3 of 11

b. combining said heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity and ~~strand cleavage activity a mismatch recognizing and mismatch directed endonuclease~~; and

c. allowing sufficient time for the percentage of complementarity to increase, wherein at least one or more sequence variants are made.

Claim 68. (currently amended) The method of claim 67 wherein said agent having ~~strand cleavage activity endonuclease~~ is added first, the agent having 3' to 5' exonuclease activity is added second, and the agent having polymerase activity is added third.

Claim 69. (currently amended) The method of claim 67 wherein said agents having exonuclease activity, polymerase activity, and ~~strand cleavage activity endonuclease~~ are added concurrently.

Claim 70. (original) The method of claim 67 in step (b) further comprising ligase activity.

Claim 71. (original) The method of claim 69 further comprising a step of, (d) adding a ligase.

Claim 72. (original) The method of claim 70 wherein said ligase is T4 DNA ligase, E. coli DNA ligase, or Taq DNA ligase.

Claims 73-77 (canceled)

Claim 78. (original) The method of claim 67 wherein said agent with polymerase activity is T4 DNA polymerase.

Padgett et al.  
Serial No.: 10/066,390  
Page 4 of 11

Claim 79. (original) The method of claim 67 wherein said agent with both polymerase activity and 3' to 5' exonuclease activity is T4 DNA polymerase, T7 DNA polymerase, E. coli Pol 1, or Pfu DNA polymerase.

Claim 80. (original) The method of claim 67 wherein said agent with both polymerase activity and 5' to 3' exonuclease activity is E. coli Pol 1.

Claim 81. (currently amended) The method of claim 67 wherein said effective amount of ~~strand cleavage activity~~ said endonuclease, and exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T4 DNA polymerase, and T4 DNA ligase.

Claim 82. (currently amended) The method of claim 67 wherein said effective amount of ~~strand cleavage activity~~ said endonuclease, and exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T7 DNA polymerase, and T4 DNA ligase.

Claim 83. (currently amended) The method of claim 67 wherein an effective amount of ~~strand cleavage activity~~ said endonuclease, and exonuclease activity/polymerase activity and ligase activity are provided by T4 endonuclease VII, T4 DNA polymerase, and T4 DNA ligase.

Claim 84. (original) The method of claim 67 wherein complementarity within a heteroduplex is increased.

Claim 85. (original) The method of claim 67 wherein complementarity is complete yielding a homoduplex polynucleotide.

Claim 86. (original) The method of claim 67 wherein diversity in a population of polynucleotides is increased.

*Padgett et al.*  
Serial No.: 10/066,390  
Page 5 of 11

Claim 87. (previously presented) The method of claim 86 wherein at least 2 different polynucleotide sequence variants are formed.

Claim 88. (previously presented) The method of claim 67 further comprising screening or selecting a population of sequence variants for a desired functional property.

Claim 89. (previously presented) The method of claim 88 further comprising selecting a sequence variant that has a different desired function property from any parent polynucleotide.

Claim 90. (previously presented) The method of claim 86 wherein said at least one heteroduplex polynucleotide has at least three non-complementary nucleotide base pairs separated by complementary nucleotide base pairs and at least 4 different sequence variants made.